

REMARKS

The Restriction Requirement

The Examiner has restated the restriction requirement previously presented in the Office Action dated June 19, 2002 (and previously traversed by Applicants in the corresponding response thereto)—without making this requirement final under 37 C.F.R. §1.143. In order to advance the prosecution of this case (without prejudice to pursuing broader protection in any divisional or continuation application), Applicants are willing to restrict the claimed invention to:

- (A) compounds where R and R¹ are optionally substituted monocyclic or bicyclic C₆₋₁₂ aryl groups; and
- (B) compounds other than those where independent R¹, R² and R³ groups can come together to form methanediylbisoxo, ethane-1,2-diylbisoxo, propane-1,3-diyl, or butane-1,4-diyl.

Pending independent claims 15 and 40, as well as relevant dependent claims, have been amended herein to reflect these concessions.

Applicants respectfully submit that the following three points raised in the restriction requirement are improper and should be withdrawn:

- (1) The Examiner's strict restriction of R¹ and R² to optionally substituted *phenyl* is unduly narrow under 37 C.F.R. §1.146;
- (2) The Examiner's exclusion of "heterocyclic ring" from the definitions of R⁴, R^{4'}, R⁵, R^{5'} and A, as well as the exclusion of "heteroaryl ring" from the definitions of R⁴, R^{4'}, R⁵ and R^{5'} is improper; and
- (3) The Examiner's exclusion of "tetrazolyl" from the definition of B is improper.

These issues are each addressed in further detail below. Applicants have herein amended independent claims 15 and 40 to reflect

1. The Restriction of R¹ and R² to optionally substituted *phenyl*

The Examiner has never explained why R¹ and R² should be limited specifically to *phenyl* rather than encompassing the more general term “aryl” originally presented in Applicants’ claim. It appears that the Examiner took the structure of the elected species, and then proceeded to recast Applicants’ claims to an overly narrow genus strictly based on the elected species. Applicants submit that such a procedure violates their right to define their invention as they see fit, and their right under 37 C.F.R. §1.146 to claim a reasonable number of species.

As for the currently pending claims, the Examiner has not (correctly) cited any invalidating prior art based on the search performed on the elected species. Accordingly, there is no legitimate basis for the Examiner to require Applicants to limit the claims to a genus so closely circumscribed to the structure of the elected species. To further elaborate on this point, the pending claims (i.e., claims 15-24, 26, 29, 30, 32-38, 40 and 42) only relate to **methods** of using the disclosed compounds to treat either chronic inflammation (claim 15 and claims dependent thereon) or diseases associated with microglia activation (claim 40 and claims dependent thereon). The only prior art that has been cited against these pending claims is the Kuhnke reference. However, Kuhnke neither discloses nor suggests that the compounds of the present invention could be used to treat chronic inflammation or diseases associated with microglia activation. Rather, Kuhnke only teaches that such compounds can be used as prostacyclin PGI₂ mimetics (therapy for thrombosis, arteriosclerosis and hyperlipidemia are the examples of specific utilities disclosed in the copy of the cited reference provided by the Examiner). Thus, because Kuhnke neither discloses nor suggests the use of these compounds to treat either chronic inflammation or disorders associated with microglia activation, the Examiner has failed to properly support either a section 102 novelty or section 103 obviousness rejection for any of the pending claims. Accordingly, having found no invalidating prior art based on a search of the elected species, Applicants are entitled to an examination of broader subject matter.

2. The Exclusion of terms “heterocycle” and “heteroaryl”

The Examiner has yet to provide any specific reason for requiring the exclusion of the term “heterocyclic ring” from the definitions of R⁴, R^{4'}, R⁵, R^{5'} and A, or for the exclusion of the term “heteroaryl ring” from the definitions of R⁴, R^{4'}, R⁵ and R^{5'}. It appears that the

Examiner's objection to these definition terms is simply based on the positions set forth in the Examiner's Section 112 objection. As such, this requirement is improper because Section 112 requirements are not relevant to the issue of Restriction. Additionally, as noted in the previous traversal of the restriction requirement, the fact that the Examiner can substantively address these claimed terms reflects that fact that the examination of these terms is not unduly burdensome (and thus not properly subject to restriction requirement in the first instance). Furthermore, as addressed separately herein (as well as in previous responses), the Examiner has not even properly supported the Section 112 objections.

3. The Exlcusion of the term "tetrazolyl"

The Examiner has provided absolutely no reason why the term "tetrazolyl" (which is a well known isostere of groups such as COOH already inlcuded within in the definition of B) should be restricted out from the definition of B. As such, the restriction requirement has not been properly supported.

The Rejection Under 35 USC § 112, first paragraph

The Office Action alleges that the disclosure does not provide enablement for compounds in which radicals R¹, R², R⁴, R^{4'}, R⁵ and R^{5'} exhibit 5 to 10-membered heteroaryl rings with 1 to 4 hetero atoms selected from N, S and O while citing several of the factors from *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). In this respect the rejection presents no rational as to why these claims are not enabled, but merely states conclusions. Specifically, it alleged that the application is not enabled, the claims are broader than the scope of enablement, and the specification lacks sufficient direction and guidance. These are mere conclusions. The rejection fails to set forth any rationale or evidence as to how the Examiner arrived at a conclusion of non-enablement.

In their previous two responses dated April 30, 2002 and October 6, 2003 Applicants have already provided a complete and compelling response to this issue. The entirety of these previous responses is incorporated herein by reference. As Applicants have nothing new to add here, the extensive arguments previously presented will not be re-entered into this response.

Claims 30 and 42

In their previous response Applicants requested that the Examiner provide separate consideration of claims 30 and 42 as they relate to the 112 rejection. As previously pointed out, the 112 rejection is not properly applied to these claims in the first instance because they recite a narrower scope for the heterocyclic groups than in the independent claims. The heterocyclic rings in each of these claims consists of a group of *specific* heterocycles that are identified by name. Yet the Examiner continues to raise this 112 objection to claims 30 and 42 without providing any basis for doing so. Clarification of the Examiner's position is respectfully requested.

Claim 30 has been amended herein to reflect the new definitions of R¹ and R², but otherwise is identical in scope to the previously presented claim.

Claim 40

In their previous response Applicants requested that the Examiner provide separate consideration of claim 40 as it relates to the 112 rejection. In this claim the substituents on the compound of formula I are defined to contain *no heterocyclic groups*—thus the basis of the rejection does not even apply to this claim. Yet the Examiner continues to raise this 112 objection to claim 40 without providing any basis for doing so. Clarification of the Examiner's position is respectfully requested.

The Rejection Under 35 U.S.C. § 112, second paragraph

The Examiner had raised various objections under Section 112 second paragraph to the format of claims 1 and 14. Applicants submit that the cancellation of claims 1 and 14 obviates the rejection.

The Novelty and Obviousness Rejections

The Examiner has raised various novelty and obviousness rejections against claims 1-40 based on the cited Kuhnke reference. Applicants respectfully submit that the cancellation of all composition claims obviates these rejections. All currently pending claims are directed to the novel use of the disclosed compounds to treat chronic inflammation and disorders associated with microglia activation—utilities that are neither disclosed nor suggested by the Kuhnke reference. Thus, Applicants respectfully request that the Examiner withdraw the

improper novelty and obviousness rejections raised against the pending method claims.

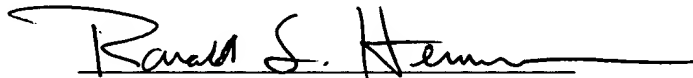
Amendment to Claim 42

Applicants have amended claim 42 to replace the phrase “a disease associated with microglia activation” with the term “chronic inflammation”. This was done to provide a proper antecedent basis for this claim, which depends upon claim 15 (which had been previously amended in the same fashion). This amendment to claim 42 merely corrects an inadvertent error.

Conclusion

Applicants submit that the pending claims are in condition for allowance, and request that Examiner reconsider the application and pass the claims to allowance in view of the submitted amendments and remarks.

Respectfully submitted,

A handwritten signature in black ink, reading "Ronald S. Hermenau". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

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